

Amendments to the Specification:

Please insert the sequence listing being filed concurrently herewith into the specification.

Please replace paragraph [0034] with the following new paragraph:

[0034] Fig. 1. Organization of the Human PEDF-R1 cDNA. A. The ORF is indicated by an open box, the predicted transmembrane (TM) domains by gray boxes (amino acid residues 7-24, 43-63, 140-159, and 325-347) and N-glycosylation sites by ticks at the top (amino acid residues 9, 39, 209 and 425). The hatched box shows the PEDF binding region p12 (amino acid residues 250-383). B. Hydrophobicity plot of the derived amino acid sequence of R1. C. Diagram showing a model for R1 topology. TM positions with preferred orientations were predicted using TMpred software. D. Amino acid sequence derived from human R1 cDNA (SEQ ID NO:3) and its alignment to adiponutrin (SEQ ID NO:27). Non conserved amino acids sequence is shown for the adiponutrin. A patatin-like region is in ***bold italic*** (amino acid residues 7-180) and TM domains are indicated by open boxes. E. Regions of R1 (p12 and C-terminal region) (SEQ ID NO:28) showing similarity with human collagen I (alpha chain). Sequences were aligned using SIM-LALNVIEW software and similarities above a threshold of 25% were considered. The range of identity between p12 regions (253-293) and several areas of human collagen I (alpha chain) (SEQ ID NO:29) is 25-71.4%. The range of identity between a C-terminal regions of R1 (450-504) and several areas of human collagen I (alpha chain) is 25-66.7%. Proline (red) rich regions, typical of collagen chain, are shown. This shows that R1 has similarity to human collagen I in the PEDF binding region (p12) and C-end region. We have shown that PEDF has binding affinity for collagen I. before (Meyer *et al.*, JBC, 277: 45400-7, 2002). This is of interest because it may represent the molecular basis for the binding affinity of R1 for PEDF. F. Alignment of partial sequences around conserved residues of R1 (SEQ ID NO:30), patatin B2 (SEQ ID NO:32) and cytoplasmic cPLA2 (SEQ ID NO:32). Active site residues of cPLA2: Ser228, Asp549, of patatin B2 Ser54 and Asp192. The homologous patatin phospholipase A (PLA) active residues of human R1 (SEQ ID NO:33) correspond to Ser47 (S47) and Asp166 (D166). The sites in Patatin B2 (SEQ ID NO:34) and cPLA2 (SEQ ID NO:35) have been obtained from crystallographic and mutational studies of these proteins (Hirschberg *et al.*,

Eur J Biochem, **268**: 5037-5044, 2001). X-ray crystallographic data clearly revealed that patatin possessed a Ser-Asp catalytic dyad and an active site similar to that observed in the catalytic domain of human cytosolic cPLA2 (Rydel *et al.*, *Biochemistry*, **42**: 6696-6708, 2003).

Please replace paragraph [0052] with the following new paragraph:

[0052] **Fig. 19.** Figure 19 provides the amino acid alignment of the mouse (Accession number BAC27476.1; SEQ ID NO:14), rat (Accession number XP_341961.1; SEQ ID NO:17) and human (Accession number AAH17280.1; SEQ ID NO:3) PEDF-R protein.

Please replace paragraph [0053] with the following new paragraph:

[0053] **Fig. 20.** Figure 20 provides the nucleic acid alignment of the mouse (Accession number AK031609.1; chromosome 7; SEQ ID NO:12), rat (Accession number XM_341960.1; chromosome 1; SEQ ID NO:15) and human (Accession number BC017280.1; chromosome 11; SEQ ID NO:1) PEDF-R cDNA.

Please replace paragraph [0246] with the following new paragraph:

[0246] With respect to the parental immunoglobulin, a useful joining point is just upstream of the cysteines of the hinge that form the disulfide bonds between the two heavy chains. In a frequently used design, the codon for the C-terminal residue of the PEDF-R part of the molecule is placed directly upstream of the codons for the sequence DKTHTCPPCP (SEQ ID NO:24) of the IgG1 hinge region.

Please replace paragraph [0392] with the following new paragraph:

[0392] Primers for screening the expression of p12 sequence were 12-forward, 5' AAC CCC TTG CTG GCG TTG C 3' (SEQ ID NO:25); and 12-reverse, 5' CCC GTC TGC TCC TTC ATC C 3' (SEQ ID NO:26). Templates were R1 cDNA, cDNAs prepared from human retina, human RPE, ARPE-19 and human TERT in PCR SuperMix reactions following instructions by manufacturer (Invitrogen).

Please replace paragraph [0393] with the following new paragraph:

[0393] Oligonucleotide primers were designed to flank the DNA fragment containing the PEDF interacting region obtained from the yeast-2 hybrid. The forward primer #1 was 5'Cacc aTG CAG CGG AAC GGC CTC CTG AAC C 3' (SEQ ID NO:6) (Cacc + gene specific). Two reverse primers were: #2, 5'Cta GTT CCT CTT GGC GCG CAT CAC C 3' (SEQ ID NO:7) (gene specific+ stop) and #3, 5'GTT CCT CTT GGC GCG CAT CAC C 3' (SEQ ID NO:8) (gene specific). PCR reactions with primers #1 and 2 were set with R1 as template to amplify p12 with a ATG and Stop codon. PCR reactions with primers #1 and 3 were set with R1 as template to amplify p12 with only the ATG codon. The PCR products were inserted into entry vectors pENTR-TOPO-D and pENTR-TOPO-SD, respectively by the TOPO reactions (Invitrogen). The p12 inserts were recombined into expression vectors pEXP-DEST-1 and pEXP-DEST-2, respectively, using LR recombinase (Invitrogen). The resulting plasmids were termed pEXP-12N and pEXP-12C and contained p12 sequences with a fusion His Tag at the N-terminus and C-terminus, respectively. The derived recombinant polypeptide from the pEXP-12N was termed p12N, and the one from pEXP-12C was termed p12C.